Quality of Life and Sexual Problems in Disease-Free Survivors of Cervical Cancer Compared With the General Population

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BACKGROUND. The purpose of this study was to identify problems related to long-term quality of life (QOL) and sexual function in cervical cancer survivors.

METHODS. The authors enrolled 860 women (median time since diagnosis, 5.86 years) with a history of cervical cancer (stage I to IVa) who had been treated at any of 6 hospitals from 1983 through 2004 and 494 control subjects selected randomly from a representative sample of Korean women. Subjects filled out a questionnaire that included the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, its Cervical Cancer Module, and additional sexual function items.

RESULTS. Cervical cancer survivors had clinically significant worse problems with social functioning, constipation, diarrhea, and difficulties with their finances than controls ($P < .01$). Survivors also reported more severe lymphedema and menopausal symptoms and worse body image, sexual and/or vaginal functioning, and sexual worry ($P < .01$). Anxiety about sexual performance was more problematic in survivors than in controls ($P < .01$), as was dyspareunia for women who received radiotherapy ($P < .01$).

CONCLUSIONS. These findings can increase the awareness of healthcare providers to the potential need for counseling and other interventions among women who have been successfully treated for cervical cancer and could help them improve their impaired QOL. ***Cancer*** **2007;110:2716–25.** © *2007 American Cancer Society.*

KEYWORDS: quality of life, sexual problems, cervical cancer, disease-free survivors.

The majority of cervical carcinoma patients are diagnosed at a relatively young age,[1,2] and most live for many years with sequelae of the disease and its treatment.[3] Cervical cancer patients treated with local treatments such as surgery or radiotherapy had long-term complications such as urinary stenosis, leg lymphedema, bowel stricture, and vaginal atrophy.[1–9] A recent study reported that cervical cancer survivors treated with radiotherapy had worse sexual functioning than did those treated with radical hysterectomy and lymph node dissection.[10]

Most of the literature concerning quality of life (QOL) and sexual functioning among cervical cancer patients has focused on those with early stage disease.[4] Few studies have examined the long-term QOL in disease-free cervical cancer survivors, and those that do compare these women with hospital-based controls rather than with the general female population.[2,5] Comparison with population-based reference data, however, can provide greater insight into the altered QOL of cancer patients and enable healthcare providers to set QOL target levels.[11]

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In this study, we compared QOL and sexual function in variously treated cervical cancer survivors with those from the general female population, and we sought to evaluate the impact of treatment-related characteristics on survivor QOL and sexual function. We hypothesized that QOL and sexual function would be poorer in cervical cancer survivors than in the general female population and that the type of cancer treatment the survivors received would have a strong impact on their QOL.

MATERIALS AND METHODS

Study Participants and Data Collection

Survivors

We identified 7028 women who had been treated for cervical cancer at a gynecological oncology department in any of 6 hospitals in South Korea from 1983 through 2004. We collected information about stage, histology, type of treatment, and other clinical characteristics from hospital cancer registries. Women were eligible to participate if they 1) had a past diagnosis of cervical cancer (stage from I to IVa), 2) were on no current cancer therapy, 3) were currently free of the disease, and 4) had no other history of cancer. Eligible subjects were contacted by telephone, and those who agreed to participate were sent the questionnaire with consent forms and a postage-paid return envelope. After reviewing the patient-reported questionnaire, we excluded subjects whose cancer had recurred or who were receiving cancer therapy at the time.

Control subjects

Our goal was to survey 500 members of the general female population distributed over 15 geographic districts. In each district, the survey was conducted in age strata according to guidelines of the 2000 Korean census. We selected villages and streets by using a probability-proportional-to-size (PPS) technique, which is widely used and is the recommended method for obtaining a representative national sample.[12] The PPS technique considers size of individual groups and corrects for differences in the probability of larger and smaller groups being sampled. The sample consisted of 775 eligible persons who were $\geq$20 years of age. Eligibility criteria included not having been a cancer patient and being able to fill out a questionnaire or communicate with an interviewer. The interviewers visited each eligible person at home or in her workplace and explained the purpose of the study. Those who agreed to participate completed the questionnaire without the interviewer being present.

All participants provided written informed consent, and the Institutional Review Board of the Korean National Cancer Center approved the protocol.

Instruments

The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 is a 30-item cancer-specific questionnaire for assessing the general QOL of cancer patients.[13] The questionnaire incorporates 5 functioning domains (physical, role, cognitive, emotional, and social), 3 symptom scales (fatigue, pain, and nausea and vomiting), global health and overall QOL scales, several single items that assess additional symptoms commonly reported by cancer patients, and the perceived financial impact of the disease and treatment.[13] The Korean version of EORTC QLQ-C30 has been validated.[14] In the present study, the reliability coefficient was 0.59 for cognitive functioning and ranged from 0.74 to 0.86 for the other multiple-item scales.

The EORTC Cervical Cancer Module (QLQ-CX24) was designed to assess the impact of common cervical cancer treatment modalities upon women's well-being.[15] This scale includes 24 items consisting of 3 multi-item scales (symptom experience, body image, and sexual and/or vaginal functioning) and 6 single-item scales. We participated in the development of the EORTC QLQ-CX24 and in the international validation study of the questionnaire[15] together with the Korean version, and we received permission from the EORTC QOL group to use the Korean version in this study before its publication. However, the Korean version of EORTC QLQ-CX24 has not been validated. The reliability coefficient for multiple-item scales of QLQ-CX24 ranged from 0.79 to 0.82 in the present study.

We assessed sexual problems with a tool used in the National Health and Social Life Survey (NHSLS),[16] a study of adult sexual behavior in the United States. This instrument incorporates 6 dichotomous response items that measure critical symptoms or problems experienced during the past 12 months by respondents who were sexually active during that time. The Korean version of NHLSLS has not been validated. However, the questionnaire has been used previously in a study of sexual activity in Korea.[17]

The full survey instrument also included sociodemographic and clinical characteristics. The utility of the full survey instrument–which comprised QLQ-C30, QLQ-CX24, a sexual function questionnaire, and a sociodemographic and clinical characteristics questionnaire–was pretested with 15 cervical cancer survivors recruited from the outpatient clinic of the Korean National Cancer Center. Results of the pretest

were satisfactory, and we used the instrument throughout this study.

Statistical Analysis

Propensity-based weighting, propensity adjustment

To adjust for observable differences between respondents and nonrespondents, we used the inverse probability of response weighting approach described by Robins and colleagues.[18] In this approach, data are further weighted according to the reciprocal of the conditional probability of being a respondent given all clinical variables (stage, time since treatment, types of treatment, and age at diagnosis), which we collected from hospital cancer registries. In addition to propensity-based weights, we used 2 different propensity scores–1 to control for differences in the characteristics between the treated and the control group and 1 to control for differences in pretreatment characteristics that led to a patient being treated primarily with surgery versus being treated primarily with nonsurgery.[19] We also tested covariate differences between the 2 groups (control subjects vs treated group, primary surgery vs primary nonsurgery group) within each propensity score quintile for validation of propensity-based weighting.

Analysis of outcomes

We compared the adjusted QOL least square mean across groups by analysis of covariance. To assess the prevalence of sexual problems across groups, we performed logistic regression for each dysfunction. For the comparison of QOL between cervical cancer survivors and the general population, we included the following variables that were plausible affecting factors for QOL in multivariate analysis as follows: age at survey (years), marital status (not married, married), educational level ($\leq$middle school, $\geq$high school), having a religion (yes, no), employment status (employed, unemployed), monthly income ($<$2000 \$US, $\geq$2000 \$US), menopausal status (yes, no), comorbidities (coronary artery disease, diabetes, chronic lung disease, musculoskeletal disease, gastrointestinal disease), regular exercise (yes, no), current smoking (yes, no), drinking status (yes, no), and the propensity score summarizing collection of different observable characteristics between cancer survivors and controls. For comparing QOL according to type of treatment, we included additional clinical factors such as treatment propensity score, stage (I-IIa, IIb-IVa), time since treatment (years), receipt of chemotherapy (yes, no), and types of local treatment (surgery, radiotherapy, surgery + radiotherapy), as well as demographic and health behavior variables. We scored the QLQ-C30 and QLQ-CX24 items according to the EORTC scoring manual.[13,15] We linearly transformed QLQ-C30 and QLQ-CX24 data to yield scores from 0 to 100; a higher score represented a better level of functioning or a higher level of symptoms. We handled incomplete questionnaires according to the developers' recommendations; when we had values for at least half the items in a scale, we recorded missing values as their mean. All statistical tests were 2-tailed, and we considered $P < .01$ to be significant. We calculated effect size to evaluate between-group differences, and we considered an effect size of >0.5 to be clinically meaningful.[20]

RESULTS

Study Participants

Of the 7028 potentially eligible cervical cancer survivors, 1085 (15.4%) died. We made multiple attempts to contact the others by postcard or telephone but were not able to reach 3127 (44.5%) of them; the most frequent reason for contact failure was a change of address or telephone number. Of the 2814 women who were contacted, 32.9% refused to participate. Of the 1887 women who agreed to participate, 898 (47.6%) returned the questionnaire. The most frequent reasons survivors gave for refusing to participate or not returning the questionnaire were that it was inconvenient (33.9%), they were too busy (18.6%), or they did not want to provide personal information (13.8%). Among those who agreed to participate, we excluded 38 whose cancer had recurred or who were receiving cancer therapy. After the questionnaires were reviewed for completeness, data from a total of 860 survivors remained for inclusion. The response rate for the 5943 potential subjects was 14.5%.

Compared with patients who responded to the questionnaire, nonresponders had their treatment longer ago ($P < .01$), and more had nonsurgery as their primary treatment ($P < .01$). Propensity weighing rendered the sample population more representative of the eligible population. We observed no differences between responders and nonresponders within each quintile, and all propensity scores were valid. Of the 775 control subjects, 494 (64%) provided complete responses.

Sociodemographic and clinical characteristics

The cervical cancer group differed significantly from the control group in several sociodemographic and health-related characteristics. After adjustment for the propensity score, however, no significant differences were evident (Table 1). Also, no significant dif-

TABLE 1
Characteristics of Cervical Cancer Survivors and Control Subjects Before and After Adjustment for Propensity Score

Characteristic	% Cervical cancer survivors* (n = 860)	% Control subjects (n = 494)	Wald F (*P*)	Wald F adjusted for propensity score† (*P*)
Age at diagnosis, y				
25–40	6.0	52.2		
41–60	59.9	34.6		
61–87	34.1	13.2	209.6 (<.001)	0.0 (.87)
Marital status				
Single	0.6	19.2		
Married	75.4	71.7		
Divorced	5.9	0.8		
Widowed	18.1	8.3	70.5 (<.001)	0.0 (.90)
Level of education				
None	4.2	2.8		
Elementary school	25.2	7.5		
Middle school	25.6	11.7		
High school	32.4	46.2		
College and above	12.6	31.8	103.3 (<.001)	0.5 (.49)
Past employment status				
Employed	33.3	44.5		
Unemployed	14.1	2.9		
Other (students, housewives)	52.6	52.6	2.5 (0.11)	0.4 (.54)
Employment status at survey				
Employed	16.4	47.0		
Unemployed	7.8	1.8		
Other (students, housewives)	75.8	51.2	99.3 (<.001)	0.1 (.72)
Have a religion				
Yes	80.8	64.4		
No	19.2	35.6	40.5 (<.001)	0.7 (.40)
Monthly income, $US				
<2000	55.2	22.9		
≥2000	44.8	77.1	124.4 (<.001)	0.2 (.68)
Menopausal status				
Yes	93.1	24.3		
No	6.9	75.7	479.3 (<.001)	1.9 (.17)
Comorbidity				
Coronary arterial disease/hypertension	23.6	6.5		
Diabetes	6.9	3.6		
Chronic Lung disease	2.2	1.2		
Musculoskeletal disease	20.7	5.9		
Gastrointestinal disease	16.4	5.7		
Other‡	5.6	1.6	78.4 (<.001)	0.3 (.59)
Regular physical activity				
Yes	52.7	44.3		
No	47.3	55.7	11.2 (<.01)	0.8 (.35)
Smoking status				
Non-smoker	90.6	93.7		
Past smoker	4.7	1.4		
Current smoker	4.7	4.9	2.5 (.14)	0.0 (.88)
Drinking status				
Non-drinker	72.5	48.8		
Past drinker	8.9	7.3		
Social drinker	18.6	43.9	83.0 (<.001)	0.3 (.55)
Histology				
Squamous cell carcinoma	85.8			
Adenosquamous cell carcinoma	2.6			
Adenocarcinoma	9.2			
Other	2.4			

(*continued*)

TABLE 1
Continued

Characteristic	% Cervical cancer survivors* (n = 860)	% Control subjects (n = 494)	Wald F (*P*)	Wald F adjusted for propensity score† (*P*)
Stage				
I–IIa	85.2			
IIb–IVa	14.8			
Time since treatment, y				
<5	43.2			
5–9	35.7			
10–14	18.8			
≥15	2.3			
Treatment				
Surgery only	56.0			
Surgery + chemotherapy	12.9			
Surgery + radiotherapy	8.0			
Surgery + chemotherapy + radiotherapy	4.8			
Radiotherapy only	10.3			
Chemotherapy + radiotherapy	8.0			

* Percentage weighted to reflect all eligible cervical cancer survivors.

† The propensity score that summarizes collection of different observable characteristics between cancer survivors and control subjects.

‡ Cerebrovascular disease, chronic liver disease, infectious disease, or renal disease.

ferences in the association of sociodemographic or clinical characteristics with primary treatment (surgery vs nonsurgery) were evident after adjustment for propensity score (Table 2).

QOL by local treatment in survivors versus control subjects

Most EORTC QLQ-C30 subscale scores were similar for survivors and control subjects, but social functioning, constipation and diarrhea, and financial difficulty scores differed significantly between the 2 groups (Table 3). Patients who received only radiotherapy reported poorer emotional functioning than did control subjects.

Survivors reported more clinically severe symptom experiences, poorer body image, lower sexual and/or vaginal functioning, and more sexual worry than the control subjects (Table 3). Regardless of type of local treatment, lymphedema and menopausal symptoms, such as hot flushes or sweats, were more severe in survivors than in control subjects, whereas peripheral neuropathy was more prominent in women who received radiotherapy.

Anxiety about sexual performance was greater in survivors regardless of the type of local treatment received, whereas dyspareunia was more problematic for women who received radiotherapy. Survivors who received both surgery and radiotherapy had increased risk for all sexuality items (except absence of sexual pleasure) than survivors who received only surgery (Table 4).

QOL by chemotherapy in cervical cancer survivors

QOL scores by chemotherapy did not differ significantly in any function or symptom subscale of EORTC QLQ-C30 or QLQ-CX24 except for lymphedema (Table 5). For sexual problems, receiving chemotherapy was associated with more dyspareunia (odds ratio [OR], 1.6; 95% CI, 1.4–2.0), anxiety about sexual performance (OR, 1.7; 95% CI, 1.4–2.1), and insufficient lubrication (OR, 1.3; 95% CI, 1.1–1.6) in multivariate analysis (Table 6).

DISCUSSION

In this study of the QOL of cervical cancer survivors compared with the QOL of a sample of the general Korean female population, the survivors reported more impaired social functioning and, as in earlier studies,[10] more severe constipation and diarrhea, urinary symptoms, and chronic leg lymphedema. Constipation and urinary dysfunction reported in earlier studies has been attributed to injury to the parasympathetic nerves during pelvic surgery,[21] and radiotherapy has been associated with chronic diarrhea.[6] It is possible that the lymphedema was related to lymph node damage that resulted from metastases. Another possibility is that the QLQ-CX24 lymphedema item may not discriminate between lower extremity swelling and deep vein thrombosis as the cause. Chemotherapy may increase the risk of deep vein thrombosis by damaging vessel walls or decreas-

TABLE 2
Independent Variables Associated With Cervical Cancer Treatment Before and After Adjustment for Propensity Score*

Characteristic	% Primary surgery†	% Primary no surgery‡	Wald F§ (*P*)	Wald F adjusted for propensity score (*P*)
Age at diagnosis, y				
25–40	27.8	8.6		
41–60	61.3	62.6		
≥61	10.9	28.8	39.2 (<.001)	3.6 (.06)
Marital status				
Not married	21.2	39.1		
Married	78.8	60.9	13.8 (<.001)	1.4 (.23)
Level of education				
≤Middle school	51.5	70.4		
≥High school	48.5	29.7	12.5 (<.001)	0.7 (.42)
Monthly income, $US				
<2000	51.1	73.3		
≥2000	48.9	26.7	15.1 (<.001)	0.7 (.41)
Employed at time of diagnosis				
Yes	65.3	72.9		
No	34.7	27.1	2.0 (.16)	0.3 (.57)
Have a religion				
Yes	80.6	82.0		
No	19.4	18.0	0.8 (.39)	0.2 (.63)
Menopausal status				
Yes	91.9	98.3		
No	8.1	1.7	6.4 (.01)	0.9 (.35)
Smoking at time of diagnosis	10.4	5.0	2.2 (.14)	0.1 (.74)
Drinking at time of diagnosis	29.2	20.0	3.9 (.05)	0.9 (.35)
Comorbidity				
Cerebrovascular disease	0.8	1.0	0.1 (.80)	0.0 (.89)
Cardiovascular disease/hypertension	23.3	24.6	0.0 (.90)	0.0 (.87)
Diabetes	6.6	8.3	0.4 (.52)	0.1 (.80)
Chronic liver disease	1.7	2.6	0.4 (.52)	0.1 (.82)
Chronic lung disease	2.2	1.9	0.0 (.86)	0.0 (.97)
Infectious disease	2.5	2.2	0.0 (.86)	0.0 (.97)
Gastrointestinal disease	17.3	12.1	2.6 (.10)	0.4 (.51)
Musculoskeletal disease	20.3	22.5	0.8 (.37)	0.2 (.67)
Renal disease	3.2	5.8	4.1 (.04)	0.6 (.44)
Stage				
I–IIa	95.5	41.9		
IIb–IVa	4.5	58.1	204.0 (<.001)	3.5 (.06)

* All estimates weighted to total eligible cervical cancer survivors (n = 5409).
† Sample size = 725 (weighted n = 4407).
‡ Sample size = 135 (weighted n = 1002).
§ F statistic based on Wald Chi-square.

ing the plasma concentration of natural coagulation inhibitors.[22]

Survivors reported significantly more menopausal symptoms, such as hot flushes and sweats, than control subjects regardless of whether they received surgery, radiotherapy, or both, even after adjustment for age and menopausal status, a finding that has been reported by others.[2,20] Those symptoms may follow from oophorectomy or radiation damage to the ovaries.[2,20] Our study also showed that survivors reported a worse body image than control subjects, possibly resulting from the cancer experience itself or its treatment.[2,7]

Our comparison of survivors with control subjects raised the possibility that radiotherapy without surgery may lead to emotional distress (This needs to be studied further.) and peripheral neuropathy. Although the peripheral neuropathy item in the QLQ-CX24 is usually used to evaluate chemotherapy-induced toxicity, it may not discriminate between chemotherapy-induced neurotoxicity and neurotoxicity following from musculoskeletal problems, post-

TABLE 3
Comparison of a Health-related Quality of Life by Local Treatment Between Cervical Cancer Survivors and Control Subjects*

		Cervical cancer survivors, (n = 860)		
	Control subjects	S†	S + R†	R†
Quality of life	(n = 494)	(n = 624)	(n = 101)	(n = 135)
EORTC QLQ-C30				
Global health status/QOL	63.6	64.2	62.2	62.2
Physical functioning	79.8	77.7	74.5	73.9‡
Role functioning	82.1	78.3	76.5	77.0
Emotional functioning	81.1	74.3§	72.7§	68.1§
Cognitive functioning	82.7	77.0§	78.1	76.3§
Social functioning	89.1	80.5§	74.6§	73.8§
Fatigue	28.3	36.9§	35.0	37.3§
Nausea/Vomiting	6.4	8.4	10.2	8.9
Pain	15.5	13.6	13.6	18.2
Dyspnea	17.1	15.5	15.5	17.2
Insomnia	16.8	20.8	20.7	17.4
Appetite loss	14.1	11.9	13.4	13.7
Constipation	13.1	35.0§	28.5§	25.7§
Diarrhea	7.1	10.8	17.0§	18.1§
Financial difficulties	11.5	23.2§	33.9§	39.5§
EORTC QLQ-CX24				
Symptom experience	6.5	14.9§	18.2§	17.0§
Body image	15.0	29.4§	40.2§	33.8§
Sexual/Vaginal functioning	11.1	23.1§	42.3§	34.4§
Lymphedema	9.0	20.1§	24.0§	18.3§
Peripheral neuropathy	11.8	20.1§	21.7§	21.9§
Menopausal symptoms	12.0	21.9§	26.7§	26.9§
Sexual worry	10.3	23.9§	40.2§	38.5§
Sexual activity	23.5	24.0	21.6	23.7
Sexual enjoyment	28.3	34.2	31.7	35.9

S indicates surgery; R, radiotherapy; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer questionnaire QLQ-C30, a 30-item cancer-specific questionnaire for assessing the general QOL of cancer patients; QOL, quality of life; EORTC QLQ-CX24, European Organization for Research and Treatment of Cancer questionnaire QLQ-CX24, the Cervical Cancer Module in the assessment tool.

* Adjusted for age, marital status, education level, employment status, religion, monthly income, menopausal status, comorbidity, propensity score, regular exercise, current smoking status, and current drinking status.

† Includes patients who did and did not receive chemotherapy.

‡ The propensity score summarizes collection of different observable characteristics between cervical cancer survivors and controls.

§ $P < .01$ indicates effect size ≥ 0.5.

surgical complications, or radiotherapy. Neurotoxicity after radiotherapy for cervical cancer has been reported previously.[8]

Sexuality is an important aspect of QOL. The effect of cervical cancer surgery on sexual function is controversial,[1,3,9,20] and different types of surgery—such as simple hysterectomy, radical hysterectomy, and nerve-sparing radical hysterectomy—are likely to have different effects. Survivors who received local treatment reported dyspareunia, which could have been related to vaginal changes following from reduced estrogen secretion.[3] In addition, psychological factors have an important role in sexual behaviors, and we found that cervical cancer survivors had more anxiety about sexual performance and sexual worry than control subjects. In addition, sexual problems reported by survivors—lack of interest in sex, dyspareunia, and especially anxiety about sexual performance—were highly associated with QOL (global health status; role, emotional, and social functioning) (data not shown).

Our finding that women who received radiotherapy had dyspareunia, persistent anxiety about sexual performance, and vaginal changes is consistent with earlier studies.[4] Radiotherapy-induced dyspareunia has been reported before and has been attributed to decreased blood flow to the vaginal walls, which increases the risk of pelvic fibrosis.[20]

Our finding that survivors who received both surgery and radiotherapy reported significantly worse sexual or vaginal problems than those treated by surgery alone agrees with findings of others[1,4] and suggests that cervical cancer patients who are undergoing combined treatment may require considerable counseling and symptom management.

Chemotherapy was also associated with sexual problems, namely dyspareunia, anxiety about sexual performance, and insufficient lubrication. Vaginal dryness could be the result of chemotherapy-induced hormone deficiency[23] and peripheral nerve damage.[24] In addition, chemotherapy side effects such as nausea and fatigue may reduce sexual functioning.[25] This understanding of QOL and sexual function, together with earlier studies, provides a more comprehensive picture of the impact of chemotherapy on QOL.

Our study on the QOL of cervical cancer survivors differs from others in several ways. First, our study included more long-term survivors who had early or advanced stage disease at diagnosis than most other studies.[1,3,9,20] Second, in contrast to some studies, ours adjusted for multiple variances, including age, chemotherapy, menopausal status, and comorbidity.[1,3,9] Third, the United States National Health and Social Life Survey questionnaires we used to evaluate sexual problems were different from the one used in previous studies.[1,3,9,20] In addition, our population differed from those of other studies in that it included relatively older women (mean age, 55 years; range, 25 to 87 years) and patients who had multiple treatment modalities, including chemotherapy.

This study had several limitations. First, although the study sample was population-based, the response

TABLE 4
Multivariate-adjusted Odds Ratio of Sexual Problems Reported by Women Who Were Sexually Active in Previous 12 Months

	Control subjects	Treatment received* by cervical cancer survivors†		
Item	(n = 494)	S	S + R	R
Lacked interest in sex, no./total no. (%)	205/389 (52.7)	286/426 (65.9)	38/52 (71.7)	46/71 (62.9)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	1.1 [0.7–1.7]	1.5 [0.7–3.5]	0.9 [0.5–1.9]
OR for women with other treatment vs S only§ [95% CI]	—	1	1.5 [1.1–2.0]‖	0.9 [0.7–1.2]
Unable to achieve orgasm – no./total no. (%)	214/389 (55.0)	257/426 (60.1)	31/52 (60.4)	40/71 (54.0)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	0.8 [0.5–1.3]	0.9 [0.4–1.9]	0.7 [0.3–1.4]
OR for women with other treatment vs S only§ [95% CI]	—	1	1.1 [0.9–1.5]	1.2 [0.9–1.6]
Experienced pain during sex, no./total no. (%)	100/351 (28.5)	182/426 (44.5)	33/52 (58.3)	39/71 (46.0)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	1.5 [0.9–2.4]	5.6 [2.3–13.9]‖	3.7 [1.7–8.3]‖
OR for women with other treatment vs S only§ [95% CI]	—	1	2.0 [1.5–2.6]‖	0.7 [0.6–1.0]
Sex not pleasurable, no./total no. (%)	182/351 (51.9)	259/426 (61.0)	29/52 (51.8)	44/71 (59.5)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	1.0 [0.6–1.6]	0.8 [0.3–1.8]	1.0 [0.4–2.1]
OR for women with other treatment vs S only§ [95% CI]	—	1	0.6 [0.5–0.8]‖	0.8 [0.6–1.1]
Anxious about performance, no./total no. (%)	103/388 (26.6)	223/424 (52.0)	38/52 (71.4)	45/69 (54.0)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	2.2 [1.4–3.5]‖	6.7 [2.8–15.9] ‖	4.1 [2.0–8.5]‖
OR for women with other treatment vs S only§ [95% CI]	—	1	2.3 [1.7–3.0]‖	1.3 [1.0–1.8]
Trouble lubricating, no./total no. (%)	110/387(28.4)	228/424 (54.2)	31/52 (62.4)	40/70 (50.0)
OR for women with cervical cancer vs GP‡ [95% CI]	1.0	1.3 [0.8–2.0]	1.5 [0.7–3.3]	1.2 [0.6–2.5]
OR for women with other treatment vs S only§ [95% CI]	—	1	1.5 [1.1–1.9]‖	0.8 [0.6–1.0]

The propensity score summarizes collection of different observable characteristics between cervical cancer survivors and control subjects. S indicates surgery; R, radiotherapy; CT, chemotherapy; no., number; OR, odds ratio; GP, general population; CI, confidence interval.

* May or may not include chemotherapy.

† Sample size, S(±CT) = 624 (weighted n = 3801); S + R (±CT) = 101 (weighted n = 605); R (±CT) = 135 (weighted n = 1,003).

‡ The model represents OR for women with cervical cancer vs controls adjusted for age at survey (years), marital status (not married, married), educational level (≤middle school, ≥high school), having a religion (no, yes), employment status (employed, unemployed), monthly income (<2000 $US, ≥2000 $US), menopausal status (yes, no), comorbidities (coronary artery disease, diabetes, chronic lung disease, musculoskeletal disease, gastrointestinal disease), propensity score, regular exercise (yes, no), current smoking status (yes, no), and current drinking status (yes, no).

§ The model represents OR for women with other treatment vs S (±CT) adjusted for age at survey (years), marital status (not married, married), educational level (≤middle school, ≥high school), having a religion (yes, no), employment status (employed, unemployed), monthly income (<2000 $US, ≥2000 $US), menopausal status (yes, no), comorbidities (coronary artery disease, diabetes, chronic lung disease, musculoskeletal disease, gastrointestinal disease), regular exercise (yes, no), current smoking status (yes, no), current drinking status (yes, no), and clinical factors such as stage (I–IIa, IIb–IVa), time since treatment (years), treatment propensity score, and receiving chemotherapy (yes, no). All estimates weighted to total eligible cervical cancer survivors (n = 5409). Sexual problem items in cervical cancer survivors are reported as weighted percentages.

‖ $P < .01$.

rate was only 14.5% (860 of 5943 potential subjects). The amount of time that passed since the cancer diagnosis (1.4 to 22 years) and the reluctance to provide personal information that is typical of Korean women contributed to the low response rate (and possibly to under-reporting of symptoms). Although more responders than nonresponders had surgery as their primary therapy ($P < .01$), we minimized that potential bias by using a response propensity weighted analysis. Second, because the study population was diagnosed over many years (1983–2004), changes in treatment policy and technical advances during that period could be a source of confounding effects. (Of special note was the widespread adoption of cisplatin after 1999.[26,27]) When we categorized the time since treatment into 3 groups (≤4 years, 5–9 years, and ≥10 years), however, multivariate analysis showed no QOL differences between them. We also controlled for differences in survival time by using treatment propensity scores, including the variable of time since treatment in multivariate analysis. Third, because we did not match treatment and control subjects by age and sociodemographic characteristics, there might have been a selection bias. However, the propensity-based weighting method allows much better control than that seen in prior studies of cancer survivors that matched on only a few characteristic such as age and education.[28] Fourth, survivors who received surgery might have received different types of surgery (eg, conization, simple hysterectomy, or radical hysterectomy) that led to different side effects, but we could not factor in surgical details because we did not know them. Finally, despite adjustment for propensity score, the stages still differed somewhat between primary surgery and primary nonsurgery (Table 2). Although the difference was not statistically significant ($P = .06$), the propensity score adjustment might not have completely overcome the originally large difference. The difference after adjustment for propensity score is impor-

TABLE 5
Health-related QOL* of Cervical Cancer Survivors Who Did or Did Not Receive Chemotherapy

	Cervical cancer survivors	
	No chemotherapy†	Chemotherapy‡
QOL	(n = 613)	(n = 247)
EORTC QLQ-C30		
Global health status/QOL	61.5	60.6
Physical functioning	74.4	71.9
Role Functioning	76.4§	70.6
Emotional functioning	73.0	68.8
Cognitive functioning	74.6	72.1
Social functioning	78.0§	72.4
Fatigue	38.8	40.1
Nausea/Vomiting	9.8	7.8
Pain	16.3	18.4
Dyspnea	19.4	18.6
Insomnia	21.2	24.5
Appetite loss	14.3	14.5
Constipation	32.0	36.4
Diarrhea	14.4	12.0
Financial difficulties	28.2§	35.9
EORTC QLQ-CX24		
Symptom experience	16.4	18.9
Body image	33.3	37.5
Sexual/Vaginal functioning	28.0	33.1
Lymphedema	19.3§	28.3
Peripheral neuropathy	22.2	22.8
Menopausal symptoms	24.2§	31.7
Sexual worry	20.2	22.4
Sexual activity	29.2	33.0
Sexual enjoyment	30.5	25.9

QOL, quality of life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer questionnaire QLQ-C30, a 30-item cancer-specific questionnaire for assessing the general QOL of cancer patients; EORTC QLQ-CX24, European Organization for Research and Treatment of Cancer questionnaire QLQ-CX24, the Cervical Cancer Module in the assessment tool.

* Adjusted for age at survey (years), marital status (not married, married), educational level (≤middle school, ≥high school), employment status (employed, unemployed), having a religion (yes, no), monthly income (<2000 $US, ≥2000 $US), menopausal status (yes, no), comorbidities (coronary artery disease, diabetes, chronic lung disease, musculoskeletal disease, gastrointestinal disease), regular exercise (yes, no), current smoking status (yes, no), current drinking status (yes, no), and clinical factors such as treatment propensity score, time since treatment (years), stage (I–IIa, IIb–IVa), and other types of local treatment (surgery, radiotherapy, surgery + radiotherapy). All estimates were weighted to total eligible cervical cancer survivors (n = 5409).

† Weighted n = 3866.

‡ Weighted n = 1543.

§ $P < .01$; effect size ≥0.5.

TABLE 6
Multivariate-adjusted Odds Ratio* (by Use of Chemotherapy) of Problems Experienced by Survivors Who Were Sexually Active During Previous 12 Months

	Cervical cancer survivors	
	No chemotherapy†	Chemotherapy‡
Item	(n = 613)	(n = 247)
Lacked interest in sex, no./total no. (%)	267/404 (66.5)	103/145 (68.9)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	1.1 [0.9–1.3]
Unable to achieve orgasm, no./total no. (%)	245/403 (61.2)	83/146 (54.8)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	0.9 [0.7–1.0]
Experienced pain during sex, no./total no. (%)	166/403 (42.4)	88/146 (57.7)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	1.7 [1.5–2.1]§
Sex not pleasurable, no./total no. (%)	244/403 (61.4)	88/146 (60.0)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	0.9 [0.7–1.02]
Anxious about performance, no./total no. (%)	208/399 (52.8)	98/146 (63.7)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	1.6 [1.3–1.9]§
Trouble lubricating, no./total no. (%)	213/402 (55.0)	86/144 (58.8)
OR for women receiving chemotherapy vs not receiving [95% CI]	1.0	1.2 [1.02–1.4]§

no. indicates number; OR, odds ratio; CI, confidence interval.

* The model represents OR for women receiving vs not receiving chemotherapy adjusted for age at survey (years), marital status (not married, married), educational level (≤middle school, ≥high school), having a religion (yes, no), employment status (employed, unemployed), monthly income (<2000 $US, ≥2000 $US), menopausal status (yes, no), comorbidities (coronary artery disease, diabetes, chronic lung disease, musculoskeletal disease, gastrointestinal disease), regular exercise (yes, no), current smoking status (yes, no), current drinking status (yes, no) and clinical factors such as treatment propensity score, stage (I–IIa, IIb–IVa), time since treatment (years), and other types of local treatment (surgery, radiotherapy, surgery + radiotherapy). All estimates were weighted to total eligible cervical cancer survivors (n = 5409). Sexual problem items are reported as weighted percentages.

† Weighted n = 3866.

‡ Weighted n = 1543.

§ $P < .01$

tant because other studies have revealed a difference in QOL between early and late stages of cervical cancer. When we compared QOL among cervical cancer survivors according to type of treatment, we considered stage as a confounding factor. Some studies,[4,7] however, suggest that QOL and sexual activity differ in early stage and late-stage cervical cancer at baseline, but these differences disappear during the first year after diagnosis. In addition, among long-term cervical cancer survivors, QOL may depend more on type of treatment than on stage. Comparison of QOL according to stage (Ia1-Ia2 vs Ib1-IIa vs IIb-IVa) with adjustment for type of treatment yielded no clinically meaningful differences in EORTC QLQ-C30 or CX24 subscales (data not shown). Moreover, stage or type

of treatment has little effect on QOL in breast cancer or stomach cancer survivors.[29,30]

Despite these limitations, this large study is important because, by characterizing the problems of women who have been successfully treated for cervical cancer, it increases the awareness of healthcare providers to the potential need for counseling and other interventions that could help survivors improve their QOL and sexual function.[2,7] Counseling could help women who are no longer physically able to have intercourse find alternative ways to express intimacy.[25]

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